STATEMENT 2, OPTION 2, VALIDATION NOT COMPLETED:

"This device is virtually identical from an infection control perspective to the [name of predicate device(s)] for which we have previously validated the reprocessing instructions. The validation has been subject to GMP inspection."

The statements submitted do not have to be verbatim, i.e., there may be minor variations.

ODE reviewers will NOT request or review the qualification tests conducted as part of the validation for 510(k) submissions unless requested by the Office of Compliance, as directed by management on a case by case basis, or as recommended in device specific guidance. Evaluation of the validation process is primarily the responsibility of OC and the field staff.

ODE reviewers have latitude to evaluate what is submitted, e.g., to determine whether the basis for the validation is relevant, or whether the summary raises serious concerns. There is a contraint to the evaluation of the summaries. There is a paucity of published specific methods or standards on validation of reprocessing instructions. FDA recommends that the AAMI TIR and FDA guidance on process validation be used as a set of principles regarding methodology from which specific protocols may be developed (see Appendix 3). Until specific methods or standards are published, reviewers are advised to use flexibility in evaluating the summaries, e.g., evaluate the fundamental methodology and principles of the tests described rather than the specifics.

Despite general notices ragarding the availability of this guidance, many applicants will not be aware of FDA's initiative in regard to labeling of reusable devices, so there will be deficiencies. Early communication over the phone with the applicant will resolve most deficiencies. Lack of a statement of status of the validation is a deficiency that can be included in an "unable to determine SE" letter. Lack of a statement on validation can also be a basis for a not substantially equivalent (NSE) determination, i.e., acceptable equivalent performance has not been demonstrated.

2. **A PMA must include a complete report of the qualification of the reprocessing instructions in the manufacturing and control section.**

The reprocessing validation will be reviewed in the same manner as the other manufacturing and control data according to Blue Book policy.

3. **An IDE should include a summary of the qualification of the reprocessing instructions, when completed, or the protocol for qualification.**

   The reviewer should use judgement when considering the extent of the data needed to document the safety of the device. Consider conditions of approval to resolve deficiencies as the default decision unless there are critical safety concerns related to infection control.

F. Person To Contact With Questions Regarding This Guidance

Any general questions regarding this guidance should be directed, in writing, to Chief, Infection Control Devices Branch, Division of Dental, Infection Control, and General Hospital Use Devices, Office of Device Evaluation, HFZ-480, 9200 Corporate Blvd., Rockville, MD 20850, or by calling (301) 443-8897.

G. Reviewer Checklist for Reprocessing Instructions

The checklist is a summary of Section C of the guidance.

#	QUESTION	Y/N
1.	Is the device (1) reusable, (2) supplied nonsterile, or (3) supplied sterile? Does the labeling commonly include reprocessing instructions? If YES to any, continue review of instructions. If NO to all, processing instructions are not needed.	
2.	Does labeling include (re)processing instructions? If YES, continue review of instructions. If NO, is there adequate justification for omission? If NO, STOP review of reuse instructions. Labeling is deficient.	
3.	Is there an instruction for cleaning (see page 4)?	
4.	Is correct microbicidal process indicated (see page 5 and Appendices 1 and 2)?	
5.	Is the process validated (see statement and information, part E)?	
6.	Is the process feasible (see page 5)?	
7.	Is the process understandable (see page 6)?	
8.	Is the process comprehensive (see pages 6-9)? • special accessories • special pre-processing handling • disassembly/reassembly • cleaning methods • cleaning/lubricating agents • rinsing • method of disinfection or sterilization • special post-process handling • reuse life • special warnings/precautions • lay use • reference to guidance documents or accessory labeling • telephone number • user qualification of deviations	
9.	Are the recommended accessories legally marketed?	

Appendix 1
Reprocessing Triage

Critical Device[1]: a medical device that is intended to enter a normally sterile environment, sterile tissue or the vasculature. A critical device poses a high risk of infection if it is contaminated with any microorganisms. A critical device must be thoroughly cleaned and sterilized before reuse. Examples of reusable critical devices include surgical instruments, rigid endoscopes, and needles.

Semicritical Device: a medical device that is intended to come in contact with mucous membranes or minor skin breaches. Mucous membranes are generally resistant to infection by moderate levels of most bacteria but may be susceptible to certain pathogens. Compromised skin presents an opportunity for infection but a sterile device is not absolutely required for a minor breach. If a semicritical device poses a high risk, or is known to be contaminated by high grade, fomite transmissible pathogens, additional processing is necessary. A semicritical device must be thoroughly cleaned and subjected to a germicidal process with a broad spectrum of activity. Sterilization is desirable, but high level disinfection is acceptable if sterilization is not practicable. Examples of semicritical reusable devices include gastrointestinal (GI) endoscopes (trans-oral and trans-rectal), and urological (GU) endoscopes (trans-urethral).

Noncritical Patient Contact Device: a medical device that comes in contact with intact skin. The risk of infection is low. The device must be thoroughly cleaned. If there is a concern regarding cross-transmission of pathogens then an intermediate level disinfectant should be used, otherwise treatment with a low level disinfectant, or in some cases thorough cleaning alone, is acceptable. Examples of these reusable devices include blood pressure cuffs, stethoscopes, and skin electrodes.

Medical Equipment: a device, or a component of a device, that does not typically come in direct contact with the patient. It may serve as a vector for cross-contamination. The same level of care is exercised as for the noncritical devices. Examples include lights, stands, and examination tables.

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[1] The term 'Critical Device' is also defined under 21 Code of Federal Regulations, Part 820, Good Manufacturing Practices for Medical Devices. The definition and its usage under GMPs is not the same as that presented above. Recognizing the potential for confusion, this document still maintains use of the term 'critical device' in order to be consistent with terminology in infection control guidance produced by the Centers for Disease Control and publications by infection control practitioners and associations.

Appendix 2
Correlation of Triage to Microbicidal Process

Category	Process
Critical	Sterilization
Semicritical	Sterilization desirable High Level Disinfection is acceptable in most cases
Noncritical	From Intermediate Level Disinfection to Cleaning depending upon patient contact, type and amount of contamination
Equipment	Same as noncritical

Note: Some allowance is stated between the type of process that is desirable and that which is minimally acceptable for semicritical and noncritical devices. This margin of tolerance is consistent with direction from CDC and infection control practitioners.[1]

All critical reusable devices must be sterilized without exception. Reusable semicritical devices should likewise be sterilized but in some cases this will not be practicable. For example, the device materials may not withstand sterilization processes, or clinical circumstances may dictate the method of choice.

Appendix 3
Summary of Validation of Reprocessing Instructions

1. Introduction

It is likely that revised GMPs will require that the manufacturer validate the design of their reusable device and the reprocessing procedures to make certain the device can be adequately reprocessed over its use life. An industry standard for validating design and processing instructions is not available. The AAMI Technical Information Report on Reprocessing of Reusable Devices provides guidance on this matter.

There is ample additional information on sterilization validation that can be directly applied to reprocessing validation. The manufacturer may refer to the FDA Sterile Medical Devices Workshop Manual, USP XXIII, other AAMI sterilization validation standards, and the literature for assistance in developing their protocols. Available FDA guidance also discusses reconditioning (cleaning and resterilizing) of returned devices.

2. Definition of Reprocessing Instructions Validation

A documented program which provides a high degree of assurance that a specific reprocessing procedure will consistently produce a device that meets predetermined specifications.

3. The Basics of Reprocessing Validation

There are several steps to a complete validation as follows:

a. Pre-qualification

Defining Product Specifications:
- Design
- Materials
- Operating Requirements

Defining Processing Specifications:
- Cleaning and Germicidal Agents
- Precleaning and Rinsing
- Packaging
- Processing Equipment
- Microbicidal Process
- Post-processing

b. Qualification of Specified Processing Equipment to be Recommended in Labeling

c. Performance Qualifications of (1) the Cleaning/Rinsing Steps, and (2) the Sterilization or Disinfection and Final Rinsing Steps
    - Processing Equipment Evaluation
    - Microbiological Challenge
    - Product Functionality Evaluation (repeated studies for reuse)
    - Residue Evaluation

d. Documentation
    - Documentation
    - QC Review and Approval

e. Re-qualification

4. Simulated and Actual Use Studies

The performance qualifications require, at a minimum, simulated testing of reprocessing of the device. The rationale for use of only simulations should be documented by the applicant and held for inspection. The simulated use test conditions should mimic the worst-case actual use conditions (e.g., extremes of contamination and reprocessing conditions over the reuse life of the product). If the applicant cannot adequately simulate actual use conditions, then the applicant should subject the device to actual use, i.e., clinical, tests to confirm the validity of the procedures.

Appendix 4
Definition of Terms

The following are common microbiological terms that a reviewer may encounter in evaluating reprocessing instructions in device labeling culled from referenced literature.[2,3,4,5] The list is not exhaustive. The terms marked with an asterisk are used in this document. Additional definitions of terms can be found in the referenced literature.

1. Antiseptic: A substance that prevents or arrests the growth or action of microorganisms on living tissue either by inhibiting their activity or destroying them. Antiseptics are regulated as drugs.

2. Bioburden: The number and types of viable microorganisms which contaminate an article; also known as "bioload" or "microbial load". When measured, bioburden is expressed as the total count of bacterial and fungal colony-forming units per single item.

3. Bioburden Based Sterilization: A sterilization process based on known levels of microbial contamination on all surfaces to be sterilized.

4.* Biological Indicator (BI): A sterilization process monitoring device consisting of a standardized, viable population of microorganisms (usually bacterial spores) known to have high resistance to the mode of sterilization being monitored.

5. Chemical Indicator: A sterilization monitoring device designed to respond with a characteristic chemical or physical change to one or more of the physical conditions within the sterilizing chamber.

6.* Cleaning: The removal of adherent visible soil (e.g., blood, protein substances, and other debris) from medical devices by a manual or mechanical process, as part of a decontamination process.

7. Death Rate Curve (or Survivor Curve): A graphic representation of the microbial death rate kinetics of a specific microbicidal agent on a defined microbial population.

8.* Decontamination: According to the United Stated Occupational Safety and Health Administration (OSHA), "the use of physical or chemical means to remove, inactivate, or destroy bloodborne pathogens on a surface or item to the point where they are no longer capable of transmitting

infectious particles and the surface or item is rendered safe for handling, use, or disposal" [29CFR1910.1030]

Note - In common usage, "decontamination" generally refers to all pathogens (microorganisms capable of producing disease or infection), not just those transmitted by human blood.

9.* Disinfectant: An agent that disinfects.

10.* Disinfection: A process that destroys pathogens and other microorganisms by physical or chemical means. Disinfection processes do not ensure the same margin of safety associated with sterilization processes. The lethality of the disinfection process may vary, depending on the nature of the disinfectant, which leads to the following subcategories:

a. High Level Disinfection: A lethal process utilizing a sterilant under less than sterilizing conditions. The process kills all forms of microbial life except for large numbers of bacterial spores.

b. Intermediate Level Disinfection: A lethal process utilizing an agent that kills viruses, mycobacteria, fungi and vegetative bacteria, but no bacterial spores.

c. Low Level Disinfection: A lethal process utilizing an agent that kills vegetative forms of bacteria, some fungi, and lipid viruses.

11.* Fomite: An inanimate object or material on which disease producing agents may be conveyed.

12.* Germicide: An agent that destroys microorganisms, particularly pathogenic organisms. Other terms with the suffix -cide (e.g., virucide, fungicide, bactericide, sporicide, tuberculocide) destroy the microorganism identified by the prefix.

13. Microbicidal Kinetics: The mathematical relationship between a condition of exposure of a known microbicidal agent to the number of specified microorganisms killed.

14. Organic and Inorganic Load: Ambient or applied inorganic (e.g. metal salts) or organic (e.g., proteins) contaminants on the surface of a medical device prior to reprocessing. The naturally occurring organic load is also known as bioburden.

15. Overkill Sterilization: A sterilization process that is

based on an arbitrarily established higher initial concentration and resistance of bioburden than that actually expected on the medical devices to be sterilized. Overkill processes typically are based upon a 10^4-10^6 colony forming unit (CFU) population of bacterial spores known to be resistant to the sterilization process.

16.* Performance Qualification: An element of the sterilization validation program consisting of selected engineering and microbiological demonstrations performed according to a predefined protocol to show process reproducibility and product acceptability.

17.* Process Residue: The substance remaining on the surface of a medical device after exposure to a decontamination or terminal process.

18. Qualification: The documented procedure of a test protocol to show compliance to an established standard or specification.

19.* Reusable Medical Device: A device intended for repeated use either on the same or different patients, with appropriate decontamination and other reprocessing between uses.

20. Sanitizer: An agent that reduces the number of bacterial contaminants to safe levels as judged by public health requirements.

21.* Spore: The dormant state of a microorganism, typically a bacterium or fungus, which exhibits a lack of biosynthetic activity and reduced respiratory activity.

22.* Sterilant: Physical or chemical agent(s) which causes sterilization.

23.* Sterile: The absolute state where all forms of life have been eliminated. In a practical sense absolute sterility cannot be proven, therefore, sterility is considered achieved when organisms are eliminated, inactivated, or destroyed such that they are undetectable in standard media in which they have previously been found to proliferate.

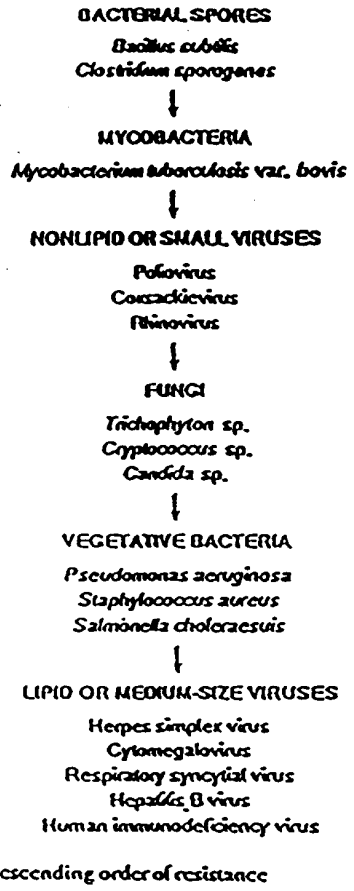
24. Sterility Assurance Level: A value indicating the probability of a microbial survivor after a sterilization process.

25.* Sterilization: An act or process which completely eliminates or destroys all forms of life, particularly microorganisms.

26.* Validation: A documented program which provides a high degree of assurance that a specific process will consistently produce a product that meets its predetermined specifications and quality attributes.

27. Vegetative: An active growth phase of a microorganism.

Appendix S (reproduced with permission)
Resistance to Germicidal Chemicals[1]



Disinfectant Activity According to Type of Microorganism[1]

Levels of disinfectant action according to type of microorganism

Disinfectant level	Killing effect[a]					
	Bacteria			Fungi[d]	Virus	
	Spores	Tubercle bacillus	Vegetative cells		Nonlipid and small	Lipid and medium size
High	+[c]	+	+	+	+	+
Intermediate	−[f]	+	+	+	±[g]	+
Low	−	−	+	±	±	+

[a] +, Killing effect can be expected; −, little or no killing effect.
[b] Includes asexual spores but not necessarily chlamydospores or sexual spores.
[c] Only with extended exposure times are high-level disinfectants capable of killing high numbers of bacterial spores in laboratory tests; they are, however, capable of sporicidal activity.
[d] Some intermediate-level disinfectants (e.g., hypochlorites) may exhibit some sporicidal activity, whereas others (e.g., alcohols or phenolic compounds) have no demonstrated sporicidal activity.
[e] Some intermediate-level disinfectants, although tuberculocidal, may have limited virucidal activity.

Appendix 6
COMPARISON OF TERMINOLOGY FDA/CDC/EPA

CDC and FDA use similar terminology pertaining to chemical sterilants and disinfectants. EPA defines these products differently. For information purposes the correlation of terms is as follows:

DEVICE RISK CATEGORY	CDC/FDA GERMICIDE TERM	EPA GERMICIDE TERM
Critical Device	Sterilant	
		Sterilant
Semicritical Device	High Level Disinfectant	
Noncritical Device	Intermediate Level Disinfectant	Hospital Disinfectant (with TB claim)
	Low Level Disinfectant	Hospital Disinfectant
		Sanitizer

Appendix 7
FDA Status of Microbicidal Processes

1. Sterilization

There are many legally marketed sterilizers. Steam, dry heat, ethylene oxide (EtO), and boiling water sterilizers are classified in the Code of Federal Regulations. Ultraviolet light sterilization is classified for water purification. Other types of legally marketed sterilizers have been found substantially equivalent to the above classified devices.

2. Disinfection

Disinfection is typically achieved by the use of liquid chemical germicides. There are a growing number of legally marketed sterilants and high level disinfectants. There are numerous legally marketed intermediate and low level disinfectants.

Appendix 8
References

1. Favero, M.S. and Bond, W.W., Chemical Disinfection of Medical and Surgical Materials. In: Disinfection , Sterilization and Preservation. 4th ed. Philadelphia: Lea & Febiger, 1991:617-641.

2. Pflug, I.J., Microbiology and Engineering of Sterilization Processes, 7th ed. Minneapolis, Environmental Sterilization Laboratory. 1990, Chapters 1-3.

3. Sterile Medical Devices, A GMP Workshop, 4th ed. HHS Publication (FDA) 84-4174.

4. Block, S.S., Definition of Terms. In: Disinfection , sterilization and preservation. 4th ed. Philadelphia: Lea & Febiger, 1991:18-25.

5. Sterilization, Questions and Answers. Manufacturing Quality Assurance Branch, CDRH, FDA.